REMARKS

Reconsideration and withdrawal of the restriction requirement are respectfully requested in view of the remarks herewith.

I. STATUS OF THE CLAIMS AND FORMAL MATTERS

Claims 1-31 are now pending. Claims 26-31 have been added, without prejudice, without admission, without surrender of subject matter, and without any intention of creating any estoppel as to equivalents. These new claims are based on the disclosure as originally filed, including the original claims, e.g., original claims 23, 25, 21, 1 and 22. No new matter is added.

It is submitted that these claims, as originally presented and presented herein, are in full compliance with the requirements of 35 U.S.C. 112. The amendment to the claims and the remarks made herein are not made for the purpose of patentability within the meaning of 35 U.S.C. §§101, 102, 103 or 112.

The August 23, 2002 Office Action required amendment of claims 23 and 25 to encompass only the subject matter elected by Applicants. However, as Applicants have made the current election with traverse, claims 23 and 25 are not amended at this time. New claims have been added to encompass only that subject matter of claims 23 and 25 that is presently elected. Should the Examiner make the restriction requirement final, claims 23 and 25 may be cancelled along with the remaining claims of the non-elected groups, e.g., upon an indication of allowable subject matter.

Indeed, to facilitate prosecution, the Inventive Entity is to be amended if the restriction requirement is maintained (by deletion of Rikke Skjot), and the specification is amended to insert a Serial Number into the blank line that appeared a page 1 of the application. No new matter is added by the specification amendment, and the Examiner is respectfully requested to act on the amendment to the Inventive Entity if he makes the restriction requirement final.

II. RESPONSE TO THE RESTRICTION REQUIREMENT

The August 23, 2002 Office Action called for restriction from among the following:

Group I Claims 1-11, 21, 24 and 25, drawn to polypeptides and method of making, classified in class 424, subclass 248.1;

Group II Claims 22 and 24, drawn to a method of vaccination using polypeptides, classified in class 424, subclass 9.2;

Group III	Claims 12-15, 18-20, 23 and 25, drawn to nucleic acids, vectors and transformed cells, classified in class 536, subclass 23.7;
Group IV	Claims 22 and 24, drawn to a method of vaccination using nucleic acids, classified in class 424, subclass 9.1.

Group I is elected, with traverse. And, as new claims 26-30 are similar to claims 23, 25, 21 and 1, it is submitted that should the Restriction Requirement stand, claims 26-30 should be added to Group I, such that applicants elect, with traverse, the claims of Group I, namely, claims 1-11, 21, 23 and 25-30.

As previously stated, should the Restriction Requirement be made final, claims 23 and 25 may be cancelled, along with the remaining non-elected claims; and, the Examiner is respectfully requested to delete Rikke Skjot as an inventor.

The Office Action states that the "inventions are distinct ... because ... Inventions I and III-IV are drawn to structurally and functionally distinct products." Office Action 3. The claims of Group I are drawn to amino acids, whereas the claims of Groups III-IV are drawn to nucleic acids which encode the amino acids of Group I. Consequently, there is a relationship between the claims of Groups I and III-IV which would make any search and examination co-extensive.

It is further stated that Groups I and II are related as product and process of use, and that as the polypeptides of Group I may be used in a materially different process (*i.e. in vitro* use for diagnosis of tuberculosis infections), the Groups are distinct. Again it is pointed out that any search of these Groups would likely be co-extensive.

Groups II and III-IV are also allegedly distinct as being "drawn to structurally and functionally distinct products." *Id.* As before, the claims of Group II are drawn to amino acids, while those of Groups III-IV are drawn to nucleic acids which encode the amino acids of Group II. Consequently, there is a relationship between the claims of Groups II and III-IV which would make any search and examination co-extensive.

The Office Action also states that Groups III and IV are related as product and process of use, and that since the nucleic acids of Invention III may be used in a materially different process (*i.e. in vitro* use for the diagnosis of tuberculosis infections in a hybrid method), the Groups are distinct. Again, it is pointed out that any search of these Groups would likely be co-extensive.

The MPEP lists two criteria for a proper restriction requirement. First, the invention must be independent or distinct. MPEP § 803. Second, searching the additional invention must

constitute an undue burden on the examiner if restriction is not required. *Id.* The MPEP directs the examiner to search and examine an entire application "[i]f the search and examination of an entire application can be made without serious burden, ... even though it includes claims to distinct or independent inventions." *Id.*

It is respectfully submitted that the claims of the present application, Groups I-IV, should be searched and examined together. As stated above, searching the claims of Groups I-IV would likely be co-extensive since the claims of Groups I-V all relate to fragments of *M. Tuberculosis*.

More specifically, Group I, e.g., claim 1, involves polypeptides, e.g., fusions of ESAT-6 and Ag85B or fusions of a T-cell epitope of ESAT-6 and Ag85B, and the claims of Group II represent methods of use of the Group I subject matter, whereas Group III represents nucleic acid molecules that encode the Group I subject matter, and Group IV represents methods of using the Group III subject matter. The subject matter of the claims has unity of invention and thus there is no undue or serious burden on the search and examination thereof in this one application.

For example, as to Groups I and III, attention is respectfully directed to Example 17 of Annex B Part 2 of the PCT Administrative Instructions (Appendix AI of the MPEP) which provides:

> Claim 1: Protein X
> Claim 2: DNA sequence encoding protein X.
> Expression of the DNA sequence in a host results in the production of a protein which is determined by the DNA sequence. The protein and the DNA sequence exhibit corresponding special technical features. Unity between claims 1 and 2 is accepted.

Clearly, there is unity of invention between Groups I and III and the search and examination of Groups I and III would be co-extensive such that these Groups should be rejointed and searched and examined in this one application.

Moreover, that the claims of Groups II and IV are the same, it is respectfully submitted, illustrates that the subject matter of Groups I-IV have unity of invention, such that there is clearly no undue or serious burden on the Examiner to search and examine all of the subject matter of all of the claims in this one application.

With respect to Groups I and II and Groups III and IV, attention is respectfully directed to Example 1 of Annex B Part 2 of the PCT Administrative Instructions (Appendix A1 of the MPEP pp. AI-39) which provides:

Claim 1: A method of manufacturing chemical substance X
Claim 2: Chemical substance X
Claim 3: The use of substance X as an insecticide
Unity exists between claims 1, 2 and 3. The special technical feature common to all the claims is substance X.

Clearly there is unity of invention between Groups I and II and between Groups III and IV. Accordingly, Groups I and II should be searched and examined in the same application; and Groups III and IV should be searched and examined in the same application.

Moreover, in accordance with MPEP 821.04 and the February 28, 1996 "Guideline on Treatment of Product and Process Claims...", 1184 TMOG 86 (March 26, 1996), the claims of Group II are subject to rejoinder with the claims of Group I, and the claims of Group IV are subject to rejoinder with the claims of Group III. Accordingly, Groups I and II should be searched and examined in the same application; and Groups III and IV should be searched and examined in the same application.

Therefore, the relationships between Groups I and II, between Groups III and IV, and between Groups I and III show that the restriction requirement should be reconsidered and withdrawn inits entirety.

Furthermore, if restriction is maintained, the relationships between Groups I and II, and between Groups III and IV, mandate that the restriction requirement should be reformulated into only two Groups (A) present Groups I and II, and (B) present Groups III and IV, with the herein election of Group I of the Office Action covering an election of herein proposed Group (A).

New claim 31 represents a method claim that is dependent on Group I claims, so that claim 31 is clearly subject to rejoinder to Group I. (Claim 31 is also responsive to the suggestion to amend claims 22 and 24 to be directed to a single invention from among Groups II and IV.) Moreover, as set forth above, it is respectfully requested that claim 31 and its subject matter be searched and examined with Group I since claim 31 and the Group II subject matter is subject to rejoinder, e.g., to have economical prosecution. That is, it is respectfully requested that if restriction is maintained that the Group II subject matter be searched and examined with the Group I subject matter.

Additionally, the Examiner's attention is respectfully drawn to MPEP §808.02 which states, "even with patently distinct inventions, restriction is not (emphasis added) required unless one of the following reasons appears:

Separate classification;

Separate status in the art; or

Different field of search[.]"

Indeed, Groups I, II and IV are all classified in class 424. Therefore, at the least, the claims of Groups I, II and IV should be rejoined on the basis of classification; and, again, at the very least on the basis of unity of invention, rejoinder under the MPEP and classification, Groups I and II should be rejoined into one Group and searched and examined in this application.

In summary, enforcing the present restriction requirement would result in inefficiencies and unnecessary expenditures by both the Applicants and the PTO, as well as extreme prejudice to Applicants (particularly in view of GATT, whereby a shortened patent term may result in any divisional applications filed). Restriction has not been shown to be proper, especially since it has been shown that the search and examination of each Group would be likely to be co-extensive, especially as there unity of invention among the Groups and Groups are subject to rejoinder, and Groups share common classification, and, in any event, search and examination of the Groups would involve such interrelated art that the search and examination of the entire application can be made without undue or serious burden on the Examiner. All of the preceding, therefore, mitigate against restriction.

Thus, it is initially respectfully requested that the restriction requirement be reconsidered and withdrawn in its entirety.

Alternatively, it is respectfully requested that at the very least there be rejoinder of Groups, e.g., reformulation of the restriction requirement such that the subject matter of Groups I and II are rejoined and searched and examined in this application, with only the subject matter of Groups III and IV withdrawn from consideration.

CONCLUSION

In view of the amendments and remarks herein, reconsideration and withdrawal of the restriction requirement, or at the very least its reformulation, are requested.

Early and favorable consideration of the application on the merits, and early Allowance of the application are earnestly solicited.

Respectfully submitted,

FROMMER LAWRENCE & HAUG LLP
Attorney for Applicants

By: _____

Thomas J. Kowalski
Reg. No. 32,147
Angela M. Nigro
Reg. No. 51,107
(212) 588-0800

APPENDIX: MARKED VERSION OF AMENDMENT

Kindly amend the application, without prejudice, without admission, without surrender of subject matter, and without any intention of creating any estoppel as to equivalents, as follows:

IN THE SPECIFICATION

Please amend the application at page 1, first full paragraph (under the "**Related applications**" section) to read as follows:

--This application is a continuation-in-part of US 09/246,191, filed December 30, 1998, which claims priority from US provisional application 60/070,488, filed 5 January 1998. Reference is also made to: the concurrently-filed US application of Andersen et al., Serial No. 09/804,980 [_____ (attorney docket 670001-2002.4)]; US application Serial No. 09/289,388 filed 12 April 1999, which is a continuation of US application Serial No. 08/465,640 filed 5 June 1995, now US Patent No. 5,955,077, issued September 21, 1999, which is a continuation-in-part of US 08/123,182 filed 20 September 1993, now abandoned, and a continuation-in-part of PCT/DK94/00273, filed July 1, 1994, published as WO95/01441, and claiming priority from Danish application 0798/93, filed July 2, 1993;US application Serial No. 09/050,739 filed 30 March 1998, which is claims priority from US provisional application Serial No. 60/044,624 filed 18 April 1997; Andersen et al., application Serial No.09/791,171, filed 20 February 2001, as a divisional of U.S. application Serial No. 09/050,739; and commonly-owned U.S. Patent No. 6,120,776.--

IN THE CLAIMS

Kindly add new claims 26-30, without prejudice, without admission, without surrender of subject matter, and without any intention of creating any estoppel as to equivalents as follows:

26. (New) A pharmaceutical composition which comprises an immunologically responsive amount of at least one member selected from the group consisting of:

(d) a fusion polypeptide which comprises a first amino acid sequence including at least one stretch of amino acids constituting a T-cell epitope derived from the M. tuberculosis protein ESAT-6, and a second amino acid sequence including at least one stretch of amino acids constituting a T-cell epitope derived from the M. tuberculosis protein AG85B, said first and second amino acid sequences optionally being fused via a linker sequence;

(e) a polypeptide comprising an amino acid sequence which has a sequence identity of at least 70% to any one of said polypeptides in (a) and at the same time being immunogenic; and

(f) a fusion polypeptide comprising at least one polypeptide or amino acid sequence according to (a) or (b) and at least one fusion partner.

27. (New) Immunogenic composition according to claim 10 or pharmaceutical composition according to claim 23, characterized in that said immunogenic composition/pharmaceutical composition can be used prophylatically in a subject not infected with a virulent mycobacterium; or therapeutically in a subject already infected with a virulent mycobacterium.

28 (New) A method for producing a polypeptide according to claim 1, comprising

(a) inserting a nucleic acid fragment which comprises a nucleic acid sequence which encodes the polypeptide, or which comprises a nucleic acid sequence complementary theretointo a vector which is able to replicate in a host cell, introducing the resulting recombinant vector into the host cell, culturing the host cell in a culture medium under conditions sufficient to effect expression of the polypeptide, and recove-ring the polypeptide from the host cell or culture medium; or

(b) isolating Ag85B and ESAT-6 from a whole mycobacterium, from culture filtrate or from lysates or fractions thereof, and fusing the polypeptides;

(c) synthesizing the polypeptide e.g. by solid or liquid phase peptide synthesis; or

(d) a combination of the methods in (a), (b) and/or (c).

29. (New) The method of claim 28 wherein the mycobacterium is *Mycobacterium tuberculosis*, *Mycobacterium africanum* or *Mycobacterium bovis*.

30. (New) The polypeptide according to claim 1 which contains a T-cell epitope of ESAT-6 and a T-cell epitope of Ag85B.

31. (New) A method for stimulating an immune response comprising administering to an animal the polypeptide of claim 1, or the immunogenic composition of claim 10 or the pharmaceutical composition of claim 26, in an amount sufficient to elicit the immune response.--

IN THE INVENTIVE ENTITY

Kindly amend the inventive entity, without prejudice, without admission, without surrender of subject matter, and without any intention of creating any estoppel as to equivalents as follows:

If the restriction requirement is maintained, then please delete Rikke Skjot as a named inventor as it is verily believed that this individual is not a named inventor of the subject matter of the claims that will be under examination if the restriction requirement is maintained and the election of Group I is accepted and only the subject matter of Group I is in the claims being examined.